REMARKS

The title of the invention has been amended to be more descriptive of the claimed invention. The specification has been amended to correct certain typographical and grammatical errors, and the claims have been amended to clarify the invention. The specification has been amended in the first sentence following the title to correct the priority claim to properly recite the relationships between the priority applications recited as well as their filing dates in accordance with 37 CFR 1.78(a)(2)(i). The specification has been amended in the paragraph beginning at page 9, line 23 to correct a reference to a recitation in priority application 08/948,197 (USPN 5,952,175), specifically at page 14, lines 12-13 of that application, regarding Northern expression analysis of PR23P. The specification has been amended in the paragraph beginning at page 18, line 25 to recite the differential expression data as shown in Example VIII rather than "Figure 3B" (which is a hydrophobicity plot). Claim 1 has been amended to recite "a naturally occurring variant of the amino acid sequence of SEQ ID NO:1 having at least 95% amino acid sequence identity to the amino acid sequence of SEQ ID NO:1". Support for the amendment to claim 1 is found in the priority application USSN 09/325,993, at p. 14, lines 14-18 of the specification. Claim 2 has been amended to delete non elected subject matter. No new matter is added by any of these amendments, and entry of the amendments is therefore requested.

Priority

The Examiner stated that the instant application is a continuation in part of application serial no. 09/325,993, filed on 6/04/99, which is a divisional of 08/948,197 filed on 10/09/97. Based on an inspection of the parent application, the Examiner has concluded that the subject matter defined in this application is not supported by the disclosure in application serial no. 09/325,993, because the instant specification is significantly different from that of the parent application (emphasis added). Accordingly, the subject matter defined in instant claims 1-6 and SEQ ID NO:1 and 2 are afforded the effective filing date of 05/29/01, which is the filing date of the current application.

Applicants' Response

Applicants submit that the Examiners' action is improper because the priority claim was properly made in full compliance with 35 U.S.C. § 120, 37 CFR 1.78 and the MPEP § 201.08. In particular, the MPEP § 201.08 states:

> Unless the filing date of the earlier nonprovisional application is actually needed, for example, in the case of an interference or to overcome a reference, there is no need for the Office to make a determination as to whether the requirement of 35 U.S.C. 120, that the earlier nonprovisional application discloses the invention of the second application in the manner provided by the first paragraph of 35 U.S.C. 112, is met and whether a substantial portion of all of the earlier nonprovisional application is repeated in the second application in a continuation-in-part situation. Accordingly, an alleged continuation-in-part application should be permitted to claim the benefit of the filing date of an earlier nonprovisional application if the alleged continuation-in-part application complies with the following formal requirements of 35 U.S.C. 120:
>
> (A) The first application and the alleged continuation-in-part application were filed with at least one common inventor;
>
> (B) The alleged continuation-in-part application was "filed before the patenting or abandonment of or termination of proceedings on the first application or an application similarly entitled to the benefit of the filing date of the first application"; and
>
> (C) The alleged continuation-in-part application "contains or is amended to contain a specific reference to the earlier filed application." (The specific reference may be in an application data sheet. See 37 CFR 1.76.)

Applicants therefore submit that the instant application is properly identified as a continuation-in-part of USSN 09/325,993, and of 08/948,197, and which contains a substantial portion of all of these priority applications. Further, that the priority claim was made in full compliance the above stated requirements, and the Examiner has provided no evidence that the earlier nonprovisional application (i.e, USSN 09/325,993) does not disclose the invention of the instant application in the manner provided by the first paragraph of 35 U.S.C. 112. Therefore, the claimed subject matter of the instant claims 1-6 must be accorded the filing date of the earliest priority application, i.e., USSN 08/948,197, filed 9 October 1997.

Objection to the Specification

The Examiner has objected to the title of the invention as not descriptive, and has required a new title that is clearly indicative of the invention to which the claims are directed. The Examiner suggested the following title: "nucleic acid encoding a progesterone receptor Complex p23-like protein". The title of the invention has been so amended. Withdrawal of the objection is therefore requested.

Claim Objections

The Examiner has objected to claim 2 as reciting non-elected SEQ ID NOs:. Claim 2 has been amended to delete non-elected subject matter. Withdrawal of the objection is therefore requested.

35 U.S.C. § 101, Rejection of Claims 1-6

The Examiner has rejected claims 1-6 under 35 U.S.C. § 101, because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The Examiner stated that the specification describes the claimed nucleic acid as encoding a progesterone receptor complex p23-like protein which shares 39% identity to human p23 (see page 9, lines 11-31). The instant specification states that the claimed sequence is expressed in various libraries, at least 67% of which are immortalized or cancerous and at least 33% of which involve immune response and that the protein of the instant invention is also expressed in neurological, respiratory, female reproductive, gastrointestinal and hematopoietic/immune tissues, (see page 9, lines 31 through page 10, line 7).

However, the Examiner stated, the instant specification does not disclose any information regarding physiologic or functional characteristics of the protein encoded by the claimed nucleic acid. Although *in vitro*, p23 has been attributed chaperone-like properties ... the function of p23 is not yet understood ... Furthermore, the fact that the protein encoded by the nucleic acid of the instant application shares 39% identity with the human p23 does not provide enough information regarding the physiological role of this protein. The claimed invention is directed to nucleic acid and its encoded protein of as yet undetermined function or biological significance. The specification does not establish a nexus between the protein of the instant invention and any disease or pathological condition. Applicants only provide the structure of the claimed nucleic acid and the protein it encodes, and an expression pattern, however, this is not sufficient to establish a specific and substantial utility for the claimed invention.

Applicants' Response

Applicants disagree that the specification does not disclose a specific and substantial asserted utility or a well established utility. The requirements for meeting the utility standard under 35 U.S.C §§ 101/112 are well established by case law.

The Applicable Legal Standard

To meet the utility requirement of sections 101 and 112 of the Patent Act, the patent applicant need only show that the claimed invention is "practically useful," *Anderson v. Natta*, 480 F.2d 1392, 1397, 178 USPQ 458 (CCPA 1973) and confers a "specific benefit" on the public. *Brenner v. Manson*, 383 U.S. 519, 534-35, 148 USPQ 689 (1966). As discussed in a recent Court of Appeals for the Federal Circuit case, this threshold is not high:

> An invention is "useful" under section 101 if it is capable of providing some identifiable benefit. See *Brenner v. Manson*, 383 U.S. 519, 534 [148 USPQ 689] (1966); *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 [24 USPQ2d 1401] (Fed. Cir. 1992) ("to violate Section 101 the claimed device must be totally incapable of achieving a useful result"); *Fuller v. Berger*, 120 F. 274, 275 (7th Cir. 1903) (test for utility is whether invention "is incapable of serving any beneficial end").

Juicy Whip Inc. v. Orange Bang Inc., 51 USPQ2d 1700 (Fed. Cir. 1999).

While an asserted utility must be described with specificity, the patent applicant need not demonstrate utility to a certainty. In *Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 USPQ2d 1094 (Fed. Cir. 1991), the United States Court of Appeals for the Federal Circuit explained:

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding lack of utility." *Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 762, 221 USPQ 473, 480 (Fed. Cir. 1984).

The specificity requirement is not, therefore, an onerous one. If the asserted utility is described so that a person of ordinary skill in the art would understand how to use the claimed invention, it is sufficiently specific. *See Standard Oil Co. v. Montedison, S.p.a.*, 212 U.S.P.Q. 327, 343 (3d Cir. 1981). The specificity requirement is met unless the asserted utility amounts to a "nebulous expression" such as "biological activity" or "biological properties" that does not convey meaningful information about the utility of what is being claimed. *Cross* v. *Iizuka*, 753 F.2d 1040, 1048 (Fed. Cir. 1985).

In addition to conferring a specific benefit on the public, the benefit must also be "substantial." *Brenner*, 383 U.S. at 534. A "substantial" utility is a practical, "real-world" utility. *Nelson v. Bowler*, 626 F.2d 853, 856, 206 USPQ 881 (CCPA 1980).

If persons of ordinary skill in the art would understand that there is a "well-established" utility for the claimed invention, the threshold is met automatically and the applicant need not make any showing to demonstrate utility. Manual of Patent Examination Procedure at § 706.03(a). Only if there is no "well-established" utility for the claimed invention must the applicant demonstrate the practical benefits of the invention. *Id.*

Once the patent applicant identifies a specific utility, the claimed invention is presumed to possess it. *In re Cortright*, 165 F.3d 1353, 1357, 49 USPQ2d 1464 (Fed. Cir. 1999); *In re Brana*, 51 F.3d 1560, 1566; 34 USPQ2d 1436 (Fed. Cir. 1995). In that case, the Patent Office bears the burden of demonstrating that a person of ordinary skill in the art would reasonably doubt that the asserted utility could be achieved by the claimed invention. *Id.* To do so, the Patent Office must provide evidence or sound scientific reasoning. *See In re Langer*, 503 F.2d 1380, 1391-92, 183 USPQ 288 (CCPA 1974). If and only if the Patent Office makes such a showing, the burden shifts to the applicant to provide rebuttal evidence that would convince the person of ordinary skill that there is sufficient proof of utility. *Brana*, 51 F.3d at 1566. The applicant need only prove a "substantial likelihood" of utility; certainty is not required. *Brenner*, 383 U.S. at 532.

The invention at issue is a polynucleotide sequence corresponding to a gene that is expressed in human tissue, in particular, uterine tumor tissue (see specification, at page 9). The novel polynucleotide codes for a polypeptide demonstrated in the patent specification to be a member of the class of molecular co-chaperones, whose biological functions are to mediate the chaperone functions of heat-shock proteins such as Hsp90. See specification, at page 2. As such, the claimed invention has numerous practical, beneficial uses in toxicology testing, drug development, and the diagnosis of disease, none of which requires knowledge of how the polypeptide coded for by the polynucleotide actually functions.

Nevertheless, Applicants disagree with the Examiners' allegations that the biological function, or role, of the human p23 protein is not understood, or that the instant PR23P protein is not likely to share that function. The function of the heat-shock protein, Hsp90, is well understood, in particular, the role of Hsp90 in protein folding of steroid receptors such as the progesterone receptor (PR). See specification, at pp. 1-2. The specification and associated references, further disclose that other proteins, such as p23 co-operate with Hsp90 in the

activation and translocation of active PR. The Weikl article, cited by the Examiner, in fact confirms that p23 functions as a "co-chaperone" for Hsp90, as well as for other proteins (see ABSTRACT and INTRODUCTION of the Weikl article, at page 685). Further, the Weikl article also confirms the specific importance of the aspartic acid-rich C-terminus of p23 for its chaperone activity. See Weikl article, at page 686, column 1, second paragraph. Thus, the Examiners' allegation that "the function of p23 is not understood" is without foundation. For example, the Examiner specifically cites the Weikl article at page 685 in support of this allegation. However, a careful examination of the INTRODUCTION discussion at page 685 reveals only a recitation at the bottom of column 2 that "the function of p23 in this context is not yet understood" (emphasis added), referring to a previous statement to the effect that other Hsp90 substrates"seem to require the presence of p23 in the Hsp90 complex for folding". Thus the fact that p23 binding is required for Hsp90 complex formation with various substrates (including PR) appears not to be in doubt , but merely the details of how it functions "in this context". Furthermore, Applicants submit that the instant application does provide sufficient information that one skilled in the art would recognize the substantial likelihood that PR23P shares the functional properties of p23. In contrast to the Examiners' contention, the specification provides substantially more evidence than the fact that PR23P and p23 share 39% sequence identity. The specification discloses that, in addition to an overall sequence identity of 39% between the two proteins, PR23P and p23 share specific chemical and structural properties, in particular, the aspartic acid-rich, C-terminus, previously identified as important in the chaperone function of p23, and similar isoelectric points. See specification, at page 9, line 23 through page 10, line 2.

In addition, the specification provides a specific and substantial asserted utility for the claimed nucleic acid in the detection and diagnosis of certain cancers that is fully supported by the priority applications, USSN 09/325,993 and USSN 08/948,197. The instant specification provides for the use of the claimed nucleic "in the diagnosis, prognosis, treatment an evaluation of therapies for neoplastic disorders, particularly squamous cell carcinoma of the lung and esophagus, and uterine leiomyoma, and immune response as a complication of cancer". See specification, at page 2, line 30 through page 3, line 2. The instant specification specifically recites at page 10, lines 8-10 that:

Transcript imaging as shown in Example VIII details the specific expression of

> SEQ ID NO:2 in neoplastic disorders, particularly squamous cell carcinoma of the lung and esophagus and uterine leiomyoma, and immune response as a complication of cancer (emphasis added).

Thus, the instant specification provides confirmation, by way of transcript imaging of PR23P expression in specific cDNA libraries, for the previously disclosed expression of PR23P in immortalized or cancerous libraries, and supporting the previously disclosed use of the claimed nucleic acid in the diagnosis of neoplastic disorders. See USSN 08/948,197 at page 2, lines 27-30; and at page 14, lines 10-12.

Moreover, the Office Action has ignored the fact that the recited polynucleotides and encoded polypeptides have specific, substantial, and credible utilities in, for example, toxicology testing in drug discovery, in particular, drug discovery related to the treatment of cancer. One of skill in the art would know that, as a part of such toxicology testing, the recited polynucleotides could be used to detect toxic side effects of drug candidates targeted to a particular polypeptide in terms of their effects on the expression of other genes and their encoded polypeptides using any of a number of methods well known in the art for studying differential gene expression, in particular, in a microarray format. See, in particular, the specification, at p. 6, lines 8-14, and at p. 13, lines 16-25. Therefore, the claimed polynucleotides meet the utility requirement of 35 U.S.C. § 101 based at least on the well-known, specific, and substantial utilities of expressed, naturally occurring polynucleotides in toxicology testing and drug discovery.

In summary, applicants submit that the Examiner has ignored well established uses of the claimed polynucleotides in toxicology testing and drug discovery and, further, has not provided sufficient evidence or sound scientific reasoning why one skilled in the art would doubt the well established utility of the claimed polynucleotide based on its membership in the gene family of chaperone proteins, specifically related to p23. Nor has the Examiner specifically addressed Applicants asserted utility for the claimed polynucleotides in the detection and diagnosis of specific cancers based on Northern analysis and transcript imaging or provided evidence or sound scientific reasoning why one skilled in the art would doubt this utility. Withdrawal of the rejection of claims 1-6 under 35 U.S.C. § 101 is therefore requested.

35 U.S.C. § 112, First Paragraph, Rejection of Claims 1-6

The Examiner has furthermore rejected claims 1-6 under 35 U.S.C. § 112, first paragraph, since the claimed invention is not supported by either a substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not no how to use the claimed invention.

To the extent that the above rejection is based on an improper rejection of the claimed invention for lack of utility under 35 U.S.C. § 101, for the reasons applicants have discussed above, this rejection is also improper and should be withdrawn.

35 U.S.C. § 102(b), Rejection of Claims 1-6

The Examiner has rejected claims 1-6 under 35 U.S.C. § 102(b) as being anticipated by Yue et al. (WO 99/19483 issued on 22 April 1999). Yue et al disclose an isolated polynucleotide encoding a human progesterone receptor complex-like protein, said polynucleotide comprising a nucleotide sequence that shares 100% (identity) to the instant SEQ ID NO:1 (sic, SEQ ID NO:2), and expression vector comprising said polynucleotide, and a host cell comprising said vector and a method of producing the encoded protein. The Examiner stated, therefore that the Yue reference clearly anticipates claims 1-6 of the instant application in the absence of any evidence to the contrary.

Applicants have previously addressed the reasons for which the claimed invention, as recited in claims 1-6, is fully entitled to the effective filing date of priority application See USSN 08/948,197 filed on 9 October 1997. Yue et al therefore does not anticipate SEQ ID NO:1 or its encoding polynucleotide, SEQ ID NO:2, and withdrawal of the rejection of claims 1-6 under 35 U.S.C. § 102(b) is therefore requested.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections/rejections. Early notice to that effect is earnestly solicited. Applicants further request that, upon allowance of claim 1, claims 7-12 be rejoined and examined as methods of use of the compositions of matter of claim 1 that depend from and are of the same scope as claim 1 in accordance with *In re Ochiai* and the MPEP § 821.04.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned at the number listed below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

INCYTE CORPORATION

Date: June 25, 2003

David G. Streeter, Ph.D.
Reg. No. 43,168
Direct Dial Telephone: (650) 845-5741

Customer No.: 27904
3160 Porter Drive
Palo Alto, California 94304
Phone: (650) 855-0555
Fax: (650) 849-8886